PA NT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 February 2001 (15.02.01)	
International application No. PCT/GB00/02259	**Applicant's or agent's file reference** P400546 WO
International filing date (day/month/year) 09 June 2000 (09.06.00)	**Priority date** (day/month/year) 10 June 1999 (10.06.99)
Applicant ANDREWES, David et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

04 January 2001 (04.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Olivia TEFY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

GB0002259

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
P400546WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/ 02259	09/06/2000	10/06/1999
Applicant		
PROVALS DIAGNOSTICS LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

MIXING APPARATUS AND METHOD OF MIXING DURING CONDUCTING AN ASSAY

5. With regard to the **abstract,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 3

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[X] because this figure better characterizes the invention.

[ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/02259

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

It is to be added references in parentheses as follows:
- line 3: Apparatus (31) comprising...
- line 5: ... that the port (9)...
- line 6: ... a sample chamber (3, 5)...
- line 7: a paddle (100)...

INTERNATIONAL SEARCH REPORT

national application No.
PCT/GB 00/02259

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-22,35

   Method of mixing a sample , paddle for mixing , sample container adapted to recieve the paddle , instrument adapted to recieve the sample container and device comprising the instrument for reading one or more samples

2. Claims: 23-29

   Device comprising an instrument for reading one or more samples with positioning of the one or more samples into a reading position

3. Claims: 30,31

   Method for determining the percentage glycation of blood

4. Claims: 32-34

   Apparatus incorporationg one or a plurality of means for breaking the surface tension of a drop leaving a first component part to enter a second component part of an apparatus

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/02259

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01F13/08 B01F13/00 G01N1/38 G01N33/72

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01F G01N B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 283 141 A (STOCKDALE TREVOR J ET AL) 11 August 1981 (1981-08-11) the whole document ---	1-4,6-9, 12,15, 19,22,35
A	US 5 272 092 A (HAMASAKI FUMITOSHI ET AL) 21 December 1993 (1993-12-21) the whole document ---	1,2,4,6, 9,12, 15-17, 19,20, 22,35
A	US 3 356 346 A (K. LANDSBERGER) 5 December 1967 (1967-12-05) the whole document --- -/--	1,2,6, 10,12, 16,19, 20,22

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 November 2000	04.01.2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hocquet, A

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 018 147 A (G SOJUZ Z MEK I KHIM OCHISTKE) 17 October 1979 (1979-10-17) the whole document	1-3,6,7, 10,12-14
A	US 4 612 291 A (DAWES DENNIS K) 16 September 1986 (1986-09-16) the whole document	1,2,6, 10-12, 19-21
A,P	WO 99 28038 A (ATTRIDGE JOHN WORTHINGTON ;CORTECS DIAGNOSTICS LIMITED (GB); STEVE) 10 June 1999 (1999-06-10) cited in the application the whole document	1-22,35
P,X	page 22, paragraph IX page 27, line 2 - line 4	30
P,A	page 25, line 8 - line 10; figures 5-9	23
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X	US 4 947 695 A (LOHR WILLY) 14 August 1990 (1990-08-14)	23-25,28
Y	column 4, line 39 - line 63; figures	26,27
Y	US 4 533 641 A (HOLT JOHN K) 6 August 1985 (1985-08-06) column 4, line 36 -column 5, line 9	26,27
A	US 3 853 010 A (CHRISTEN U ET AL) 10 December 1974 (1974-12-10) column 6, line 35 -column 7, line 55; figures	26,27
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X	US 4 407 961 A (SANDERS JAMES L) 4 October 1983 (1983-10-04) column 4, line 45 -column 5, line 24	30
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 914 023 A (PHILO ROGER) 3 April 1990 (1990-04-03) column 2, line 34 - line 51; claim 1	31
X	WO 98 43739 A (BIOSITE DIAGNOSTICS INC) 8 October 1998 (1998-10-08) page 15, line 9 - line 10 page 17, line 3 - line 29; figure 1A	32,33
X	US 4 254 083 A (COLUMBUS RICHARD L) 3 March 1981 (1981-03-03) column 1, line 35 -column 2, line 13 column 3, line 26 - line 47; claims 1,7	32,33

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/02259

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/02259

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(12) INTERNATIONAL AP ATION PUBLISHED UNDER THE PATEN OPERATION TREATY (PCT)

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International Bureau

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(25) Filing Language: English

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(30) Priority Data:
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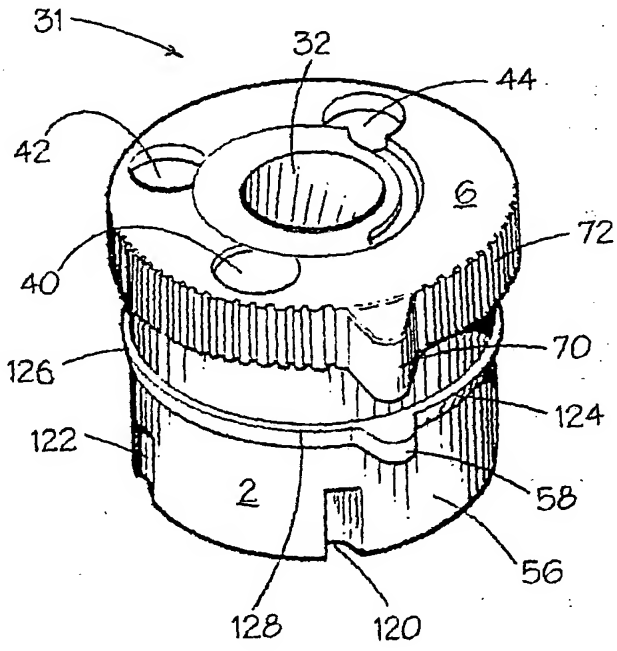
(74) Agent: **W.P. THOMPSON & CO.**; Coopers Building, Church Street, Liverpool L1 3AB (GB).

[Continued on next page]

(54) Title: MIXING APPARATUS AND METHOD OF MIXING



(57) Abstract: Apparatus, instrument, device and a method of mixing for conducting an assay. Apparatus comprising a first and second inlet and an inlet port accommodating a filter and/or binder retaining means, the inlet port moveable relative to first and second inlets such that the port can be brought into liquid communication with each inlet, and a sample chamber comprising a paddle wich undergeos a reciprocating motion.

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

DESCRIPTION

MIXING APPARATUS AND METHOD OF MIXING

The present invention relates to an improved mixing apparatus and a method of mixing.

More particularly it relates to an improved apparatus, instrument and device for conducting an assay and the assay methodology.

In a particularly preferred embodiment it relates to a device suitable for use in assaying analyses, for example glaciated proteins, in samples such as, for example, blood.

A person skilled in the art will however appreciate that the principle behind the invention can be applied to solve a mixing problem in a number of different apparatus, instruments or devices.

The applicant has developed an apparatus, instrument and device for conducting an assay as disclosed in PCT/GB98/03586. The apparatus comprises a first inlet, a second inlet, and an inlet port, the inlet port being moveable relative to each of said first and second inlets such that the port can be brought into liquid communication with each inlet in turn as required, the inlet port accommodating a filter means and/or a binder retaining means.

In the course of conducting an assay to, for example, determine the presence or absence of one or more analyses in a sample, the sample is separated into a first component fraction and a second component fraction,

the second component fraction being obtained by eluting a component "held" on the binder retaining means from the binder retaining means.

The applicant has determined that the elution step in which the elutant fills the second inlet under gravity, gives a non-homogenous sample (due to the formation of an elution gradient in the second inlet) which results in inaccurate readings when the sample is "read" in a measuring instrument, such as, for example, an instrument comprising a microprocessor operable via a keypad, one or more light emitters and one or more light detectors, a display and driver, an analogue to digital convertor and means for connecting the instrument to a power source.

It is an aim of the present invention to provide a simple method for making a gravity fed fraction homogenous and more particularly to provide a modified apparatus, instrument and/or device capable of performing such a method.

In accordance with a first aspect of the present invention there is provided a method of mixing a sample in a chamber comprising positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.

It is another and independent aim of the present invention to provide an apparatus, instrument or device, capable of mixing a sample for an assay in which an analyte is detected by a spectrophotometric means and/or a component for use in achieving this aim.

According to a further aspect of the present invention ther is provided, a paddle comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

Preferably the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.

Preferably the paddle is T shaped.

More preferably the fluid moving surface has an opening formed therein through which a light beam can pass.

In one embodiment, the paddle comprises a magnetic material and is caused to undergo a reciprocating motion by an electromagnetic means such as a solenoid.

Of course other mechanisms could be used to effect a reciprocating motion. For example, the paddle could comprise a piezoelectric material and be caused to undergo a reciprocating motion using a localised current.

According to yet a further aspect of the present invention there is provided a sample container adapted to receive a paddle said paddle being mounted in or over said sample container such that the paddle can undergo a reciprocating motion in the container.

Preferably the sample container comprises a base with sides extending therefrom to define a chamber, said sides comprising means, for example a pair of slots, which support the paddle.

Preferably the sample container is an apparatus comprising an optical chamber.

More preferably the sample container is part of a carousel or cassette.

According to yet a still further aspect of the present invention there is provided an instrument adapted to receive a sample container comprising a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the container.

Preferably said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means, for example a solenoid.

According to yet a still further aspect of the present invention there is provided a device comprising a reading instrument comprising means for driving a paddle in a reciprocating manner in an apparatus comprising an optical chamber.

An example of an apparatus and instrument which can be adapted in accordance with the present invention are described in International application PCT/GB98/03586.

The apparatus and instrument described in PCT/GB98/03586 are susceptible to a number of other problems common to devices which are used in assays. Thus, a separate and unrelated problem with a device of the general type described in PCT/GB98/03586, namely one in which a sample or samples are presented to an instrument for reading, is one of accurately positioning the sample relative to, for example, one or more of the light

emitters and one or more light detectors which make up the reading means if reading errors are to be avoided or at least minimized.

Thus it is an independent aim of the present invention to provide a device which enables accurate readings to be taken.

According to this independent aspect of the present invention there is provided a device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

The two phased recognition preferably utilises at least two independent micro switches.

A first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.

A first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection. Preferably the element on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly. The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board.

A second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise (as opposed to general) location on the instrument.

In one embodiment the two members of the switch are a notch in the outermost wall of the apparatus, more particularly a carousel or cassette type apparatus, and a resilient member or arm on the instrument. When the carousel or cassette type apparatus moves into position the resilient member or arm moves from a position in which the member is biased to its unbiased position thereby deactivating the switch.

This two stage recognition makes assembly easier and increases the robustness of operation. It also improves the ease of use.

In the case of a carousel device of the type disclosed in PCT/GB98/03586, it is preferred that there are a plurality of such switches. More preferably there are four such switches located 90° apart.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is how to achieve good readings when quantifying two different fractions.

For example in the case of diabetes management it is desirable to determine the percentage of blood haemoglobin (Hb) that is glaciated. This means two assay results need to be obtained and a comparison made between them. For example between glaciated and non glaciated haemoglobin.

Traditionally analyses are measured at a peak frequency. In the case of glaciated proteins containing haem pigment this peak frequency is around 405nm. The applicant has determined that there are significant advantages

to be gained by making the measurements off peak, and in the case of glaciated haemoglobin protein, at between 415-460nm, more particularly still at about 440nm. This frequency range corresponds to be shoulder of the absorbance verses wavelength graph for haemoglobin. The 440 nm figure is the preferred wavelength. This extends the linear response to cover a wider and hence more useful range of haemoglobin concentrations.

According to this independent aspect of the present invention there is provided a method for determining the % glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glaciated proteins, and a second component containing the one or more glaciated proteins, and detecting/quantifying the analyte by spectrophotometric means at between 405 nm and 460 nm, more preferably at about 440nm.

The "off peak" measurement avoids complicated calibration procedures, both in production and on-going in the field. It is essential for the performance of an instrument and when comparing tests between instruments that there is a linear response between measurement and concentration of absorbing substance. It is equally important that the range of linear response is wide enough so that measurement of, for example, both glaciated and unglycated fractions can be made on a linear portion of a response curve. The reason for this is that the slope of the linear response will vary for a numb r of reasons from instrument to instrument. Also the

slope of the linear response will also vary within an instrument as a function of temperature or other environmental factors. However, the nature of the calculation of % glycation is such that, within a given instrument, the slope of the response cancels out. Variations in slope do not therefore effect the result either within an instrument or between instruments, as long as significant change does not occur over the period of an assay. Any remaining variation between instruments can therefore be equalised using a calibrated offset established during initial set up at manufacture.

The use of a narrow band of wavelength produces a linear response but as this nears the absorbance maximum of haemoglobin the range of response is reduced. This is because at this point the system is at its maximum sensitivity. The selection of suitable band pass filters away from the absorbance maximum de-sensitises the system and extends the working range of the response allowing the elimination of slope factors described above. The reduced sensitivity is then offset by achieving a high signal to noise ratio on the detector electronics.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is ensuring accuracy of readings and keeping critical values (CV's) to a minimum.

The applicant has demonstrated that a major factor effecting critical values is ensuring all of the sample is collected for measuring. Thus where small volumes are measured as much as 8% of the total volume can be lost

in a single drop.

According to this independent aspect of the present invention there is provided an apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.

In one embodiment the means comprise a web or like member situated between the first and second components parts.

More preferably the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets, said inlet port being funnel shaped and accommodating a filter means or binder retaining means, said web being situated across the outlet of said funnel.

A separate and unrelated problem with a device of the general type described in PCT/GB98/03586 is the problem of ensuring the apparatus is firmly held in position in the apparatus when readings are to be taken.

The Applicant has resolved this problem by careful design of the apparatus and instrument.

Thus in one embodiment the carousel apparatus comprises a tapered circumferential ring and the instrument comprises spring clips which pull the carousel downwards preventing wobble.

According to this independent aspect of the present invention there is provided a device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument,

wherein the apparatus is held firmly in position in the instrument by means of spring clips.

The main invention and various independent aspects of the invention will now be described, by way of example only with reference to a device of the general type described in PCT/GB98/03586 and a method of assaying glaciated and non glaciated haemoglobin fractions.

FIG. 1 is a perspective view of an apparatus according to one aspect of the invention;

FIG. 2 is a partial sectional view of the Fig. 1 apparatus;

FIG. 3 is a perspective view of the base portion of the apparatus of FIG. 2 showing the paddle of the invention; and

FIG. 4 is a perspective view of an instrument for use with an apparatus as illustrated in FIGS 1 to 3.

Referring to Figs. 1 and 2 the carousel apparatus 31 comprises a base section 2 of clear plastics (shown in detail in Fig. 3), a top portion 6 and a funnel portion 32. The funnel portion 32 is made of a hydrophobic plastics and has a relatively large aperture to simplify emptying of reagents therein. It has an outlet 34 which directs the liquid into the optical chambers 3 and 5 when the apparatus is rotated in an instrument. The outlet 34 includes a frit (not shown) which frit serves to retain particles such as, for example, an amino phenyl boronate agarose affinity matrix. The funnel 32 which serves as an inlet port has an annular rim 36 with a recessed portion 38. The rim

36 partially overlies apertures 40, 42 and 44 formed in the top portion 6 of the apparatus such that tubes vertically disposed in the apparatus cannot pass through the respective apertures until the apertures are aligned with the recessed portion 38 of the annular rim. Projecting from the underside of the funnel is a stem 48 with a female mating member via which the apparatus 31 is connected to the instrument 24 which has a male member 50 adapted to engage it. The male member 50 holds the funnel in a fixed position relative to the instrument 24 such that the base portion 2 and top portion 6 of the apparatus 31 which together form a carousel rotate around the funnel, the annular rim 36 of the funnel serving as a guide means.

The base portion 6 of the apparatus is made of a clear plastics, is generally annular in shape and is divided into a plurality of compartments. As can be seen from Fig. 3 there are two optical chambers 3 and 5, a third chamber 4, for receiving waste from a wash step, which third chamber is disposed between optical chambers 3 and 5, and three additional chambers 40', 42' and 44' each housing a reagent tube. These chambers 40', 42' and 44', which are disposed below apertures 40, 42 and 44 in the top portion 6 of the apparatus 31, are arranged so that the reagent tubes are presented to the user when the carousel is in the appropriate position in use. The optical chambers have a curved outer wall 52 and a curved inner wall 54 of optical quality, which help focus light from the LED's of the instrument 24 through the sample in the chamber to photodiodes at the other side thereof.

Each optical chamber 3, 5 can be brought into liquid communication with the outlet 34 of the funnel inlet port 9. Alternatively, the optical chambers can be recessed. Extending outwardly from the outermost wall 56 of the base portion 2 is a guide member 58 which sits within a circumferential channel member 60 formed on the outermost wall 62 of the annular recess 64 of the instrument 24. A communicating channel 66 which extends from the channel member 60 in outermost wall 62 to the top face 68 of the instrument 24 allows the guide member 58 to be inserted into the channel member 60 when the apparatus 31 is connected to the instrument 24.

A projecting member or tab 70 on the knurled edge 72 of the top portion 6 acts as an indicator means, denoting the position for locating the apparatus on the instrument and serves to assist in the turning of the apparatus.

The base portion 2 is connected to the top portion and the funnel portion sits in a channel 76 formed by a step on the top surface 78 of the top portion 6.

The instrument illustrated in Fig. 4 has been designed for use with a basic apparatus as herein before described. The instrument is provided with a power management and monitoring circuit so that the instrument can be connected to, for example, an external dc supply or a car battery. Additionally, the instrument is provided with a communication system such as, for example, a RS232 thereby providing means for sending and receiving

instructions and down loading data.

Significantly, the means for receiving the apparatus is an annular recess 64 in the instrument which is defined by a floor, an outermost sidewall 62 and an innermost sidewall 80.

The floor of the annular recess comprises a ramp 82 on a part thereof. Within the outermost sidewall 62 of the annular recess is a channel member 60 and extending therefrom to the top surface a connecting channel 66.

In use the basic apparatus is inserted into the annular recess 60 by aligning guide member 58 of the apparatus with connecting channel 66 so that the apparatus is connected to male mating member 50 via its female mating member 48. The guide member 58 can thus enter channel member 60 such that it can be rotated. On rotation a first tube is directed up the ramp 82 and out of its aperture 44 since the recessed portion 38 of the annular ring 36 is aligned with the aperture. In this position the outlet 34 is in liquid communication with the first optical chamber 3 and the first step of the assay can be conducted. By turning the apparatus through a further 90° a wash solution is presented through aperture 42 for use and then on turning the apparatus though a further 90° tube 40, the eluting solution, is presented. In this manner the appropriate reagents are presented for each step of the assay process.

Having briefly described the favoured basic apparatus and instrument there follows a more detailed look at the improvements.

When tested an apparatus as described in PCT/GB98/03586 showed a critical value in the order of 6-7%. This was found to result primarily from an elution gradient forming when the glaciated fraction was eluted off the solid phase. In fact, it was found that the glaciated fraction was eluted off in a decreasing concentration as the elution buffer percolated into the optical chamber 5. Tests indicated that the first concentrated drops emerging from the funnel 32 collected in the corners of the optical chamber 5 and did not mix sufficiently with the more dilute drips that followed. As a result measurements taken before mechanical mixing of the solution showed poorer precision and an "off set" from those recorded post mixing.

To overcome this problem it proved necessary to introduce a mixing step.

However traditional methods proved unsuitable. Thus, for example, the apparatus could not be shaken without fear of damage to the instrument, and the use of a rotating flea or oscillating ball bearing could damage the optical chamber.

The applicant solved the problem using a paddle 100. A number of approaches were used:

Retention of a stirring device was seen as the major issue to be resolved. Attaching a stirring component to the side walls of the optical chamber was seen as a possible approach to overcome this problem. Two alternatives were investigated: In one embodiment the paddle was

clipped over the side walls of the optical chamber and the paddle was made to vibrate in the direction of the optical axis using an electromagnet. A hole in the centre of the paddle provides a path for the light from the LED.

In another embodiment the paddle was clipped over one side of the optical chamber 5 and was made to vibrate at right angles to the optical axis away from the light path.

Both these embodiments provided adequate mixing once a resonant frequency was found by adjusting the frequency of an oscillator driving an electromagnet. Though attractive there were still a number of problems with this approach.

As the paddle must retain stiffness a significant amount of energy was required to generate the oscillation. This would have implications for any battery operated instrument.

Furthermore resonant frequencies vary from component to component and with the liquid level within a chamber. Some means of scanning the frequencies would thus be required to hit resonance and thus ensure adequate mixing. Since both components also had a 3-dimensional shape forming was required increasing costs.

An alternative approach of using a flat paddle overcame the problems associated with the oscillating approach described above.

Thus in a preferred embodiment and as illustrated in Fig.3 a metal paddle 100 was retained in grooves 101 formed by building-up the side walls

102, 104 of the optical chamber 5. The paddle was able to reciprocate with minimal friction and could be forced to swing through the solution, along the direction of the optical axis, using an electromagnet positioned below the photodiode on the outer circumference of the platten moulding (described hereafter). A hole 106 is provided to enable the light from the LED to reach the detector.

As very little force is necessary to move the paddle, significantly less energy is required to drive the electromagnet. Experiments have shown that fewer than 10 swings of the paddle are required to produce a visually homogenous solution from a layered dye-water starting solution.

Effective retention of the paddle has been demonstrated by positioning a web (not shown) on the underside of the top moulding 6, just above the centre of the paddle.

Another improvement relates to the use of 2 micro-switches in a phased approach. This allows the precise unambiguous detection of the apparatus 31 in the instrument 24. One switch (not shown) at each of four locations is activated by a feature 58 (in this case also the guide member) on the circumference of the plastic well as it rotates. This depresses a board mounted micro-switch (not shown) via a rocker arm assembly (110, 112, 114 & 116) at each of the four operating positions (Fig. 4). The rocker arm actuation overcomes any error in the horizontal location of the switch on the circuit board (not shown). This constitutes the first phase of detection.

The second phase of detection is provided by a micro-switch which is activated by the operation of a ratchet arm not shown with a respective notch or notches 120, 122, (only two of the four are visible) in the outermost wall 56 of the carousel. A flange 131 extending from the ratchet arm contacts a switch on the instrument. The ratchet arm is biased such that when the carousel is in one of the four operating positions it moves into a notch in the carousel, deactivating the switch but when it is not in one of these positions it is acted against by the outermost wall 56 of the carousel causing the switch to be activated. These notches are preferably shaped to allow rotation in one direction only. These switches are only de-activated when the instrument and apparatus are in an exact location. The two phased approach makes assembly easier, increases robustness of operation and improves ease of use.

Finally another improvement relates to the arrangement used to overcome a 'wobble' problem. Any movement, however small, between the carousel and instrument can alter the path of light during reading. By modifying the carousel and instrument to provide a lock facility the reading problem was overcome.

In one embodiment the carousel comprises (Fig.1) a circumferential ring 124 comprising an inclined surface 126 and a flat surface 128.

The instrument 24 which receives the carousel comprises a casing 130, a printed circuit board 132 onto which is mounted a plateen 134 and a

hold down 136 comprising four spring clips 138, 140, 142, 144. When the carousel is inserted into the instrument, the spring clips ride up the inclined surface 126 and their claws lock against the flat surface 128.

CLAIMS

1. A method of mixing a sample in a chamber (3, 5) comprising positioning a paddle (100) in the sample and causing said paddle to undergo a reciprocating motion.

2. A method a claimed in claim 1 wherein the paddle is of a magnetic material and comprises a liquid moving surface and means for supporting the paddle in or over the chamber and said paddle is caused to undergo a reciprocating motion by the action of an electromagnetic means.

3. A method as claimed in claim 2 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface which arms sit in a pair of slots in sides extending from a base which defines the chamber.

4. A method as claimed in either claim 2 or 3 which further comprises detecting an analyte in said sample by passing a light beam from a light emitter through said chamber and an opening (106) formed in the liquid moving surface of said paddle to a light detector.

5. A method as claimed in claim 4 wherein the sample is glycated haemoglobin and is detected by a spectrophotometric means at between 405 nm and 460 nm.

6. A paddle (100) comprising a liquid moving surface and means for supporting said paddle in or over a chamber such that the paddle can undergo a reciprocating motion in the chamber.

7. A paddle as claimed in claim 6 wherein the means for supporting the paddle in or over the chamber comprises a pair of arms extending from the liquid moving surface.

8. A paddle as claimed in either claim 6 or 7 wherein the paddle is T shaped.

9. A paddle as claimed in any of claim 6,7 or 8 wherein the liquid moving surface has an opening (106) formed therein through which a light beam can pass.

10. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a magnetic material.

11. A paddle as claimed in any of claims 6 to 9 wherein the paddle comprises a piezoelectric material.

12. A sample container comprising a chamber (3, 5) adapted to receive a paddle (100), said paddle being mounted in or over said chamber such that the paddle can undergo a reciprocating motion in the chamber.

13. A sample container as claimed in claim 12 comprising a base with sides extending therefrom to define the chamber, said sides comprising means which support the paddle.

14. A sample container as claimed in claim 13 wherein said means which support the paddle is a pair of slots in said sides.

15. A sample container as claimed in any of claims 12-14 in which said chamber is an optical chamber.

16. A sample container as claimed in any of claims 12-15 which is a carousel or cassette.

17. A carousel as claimed in claim 16, for use in an assay in which a sample is separated into a first component fraction and a second component fraction, which fractions are presented to an instrument, comprising a first inlet which is or leads to a first component fraction collection chamber, a second inlet which is or leads to a second component fraction collection chamber, and an inlet port accommodating a filter means or a binder retaining means, said inlet port being movable relative to each of said first and second inlets such that the inlet port can be brought into liquid communication with each first and second inlet in turn as required.

18. A sample container as claimed in claim 16 which is a carousel comprising a base portion having a plurality of chambers including first and second inlets, a top portion which together with the base portion forms the carousel, and a funnel portion including an inlet port, said carousel being rotatably mounted about said funnel portion.

19. An instrument adapted to receive a sample container comprising a chamber adapted to receive a paddle, said instrument comprising means for causing said paddle to undergo a reciprocating motion in the chamber.

20. An apparatus as claimed in claim 19 in which said means for causing said paddle to undergo a reciprocating motion is an electromagnetic means.

21. An apparatus as claimed in claim 20 wherein said electromagnetic means is a solenoid.

22. A device comprising an instrument capable of detecting an analyte in a sample which is presented thereto in a sample container comprising a chamber adapted to receive a paddle said paddle being mounted in or over said chamber such that said paddle can undergo a reciprocating motion when initiated by said instrument.

23. A device, comprising an instrument for reading one or more samples, and an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.

24. A device as claimed in claim 23 in which a first switch informs the instrument that the apparatus is within range and a second switches confirms precise alignment.

25. A device as claimed in claim 23 or 24 wherein a first micro switch on the instrument is activated by an "element" on the apparatus and this constitutes the first phase of detection and a second switch on the instrument serves as the "fine tune" and is activated when the instrument reaches a precise location on the instrument.

26. A device as claimed in claim 25 wherein the "element" on the apparatus is a projecting member which depresses a board mounted micro-switch via a rocker arm assembly.

27. A device as claimed in claim 26 wherein the two members of the switch are a notch in the outermost wall of the apparatus, and a resilient member or arm on the instrument.

28. A device as claimed in claim 27 wherein the apparatus is a carousel or cassette type apparatus.

29. A device as claimed in claim 28 comprising four switches located 90° apart.

30. A method for determining the percentage glycation of blood comprising separating a blood sample into a first component fraction containing one or more non glycated proteins, and a second component containing the one or more glycated proteins, and detecting/quantifying glycated haemoglobin by spectrophotometric means at between 405 nm and 460 nm.

31. A method as claimed in claim 30 wherein the detection/quantification of glycated haemoglobin is measured at about 440nm.

32. An apparatus incorporating one or a plurality of means for breaking the surface tension of a drop to ensure it leaves a first component part and enters a second component part of an apparatus.

33. An apparatus as claimed in claim 32 in which the means comprise a web or like member situated between the first and second component parts.

34. An apparatus as claimed in claim 32 or 33 wherein the apparatus is of a type in which an inlet port is movable relative to each of first and second inlets which are or lead to first and second collection chambers, said inlet port being a funnel and accommodating a filter means or binder retaining means, said web being situated across an outlet of said funnel.

35. A device comprising an instrument for reading one or more samples and an apparatus for presenting the one or more sample to the instrument, wherein the apparatus is held firmly in position in the instrument by means of spring clips.

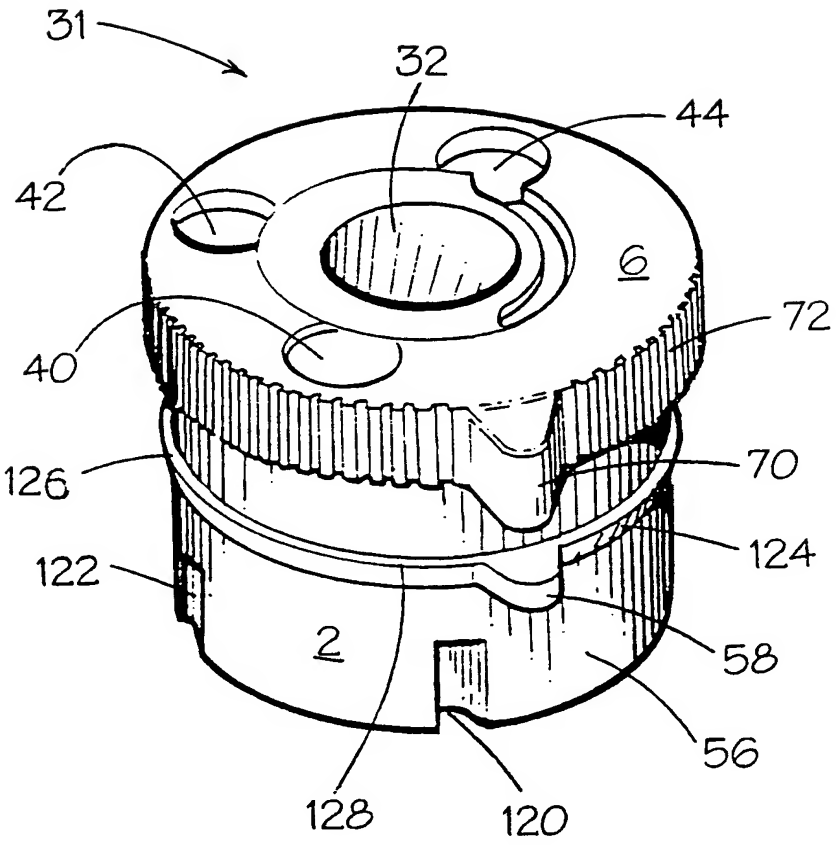

FIG. 1.

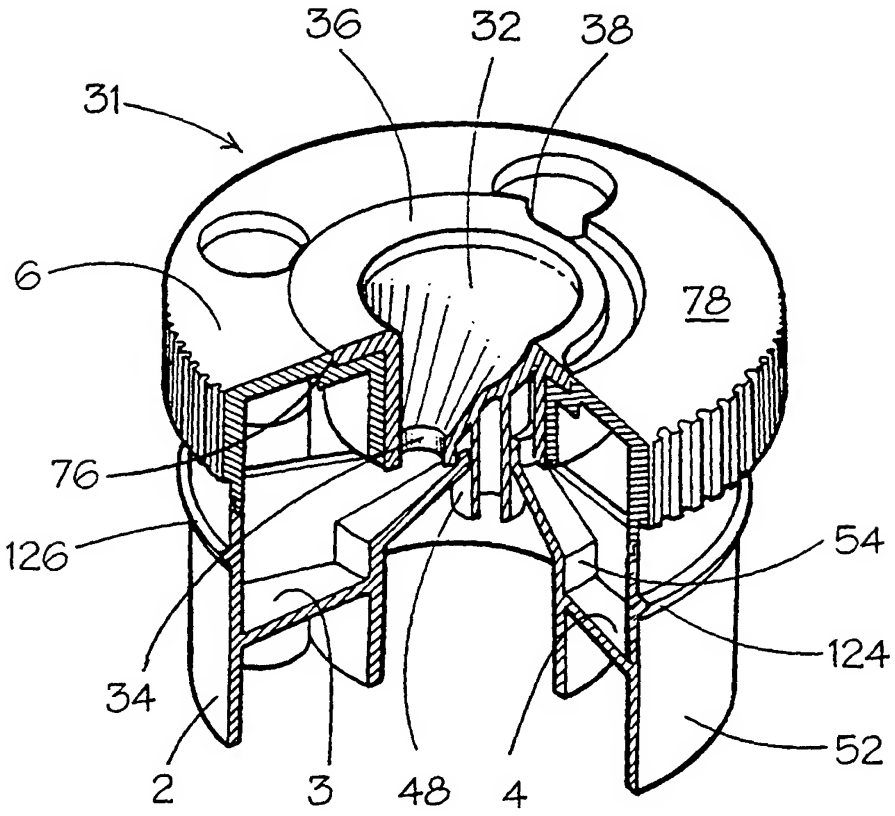

FIG. 2.

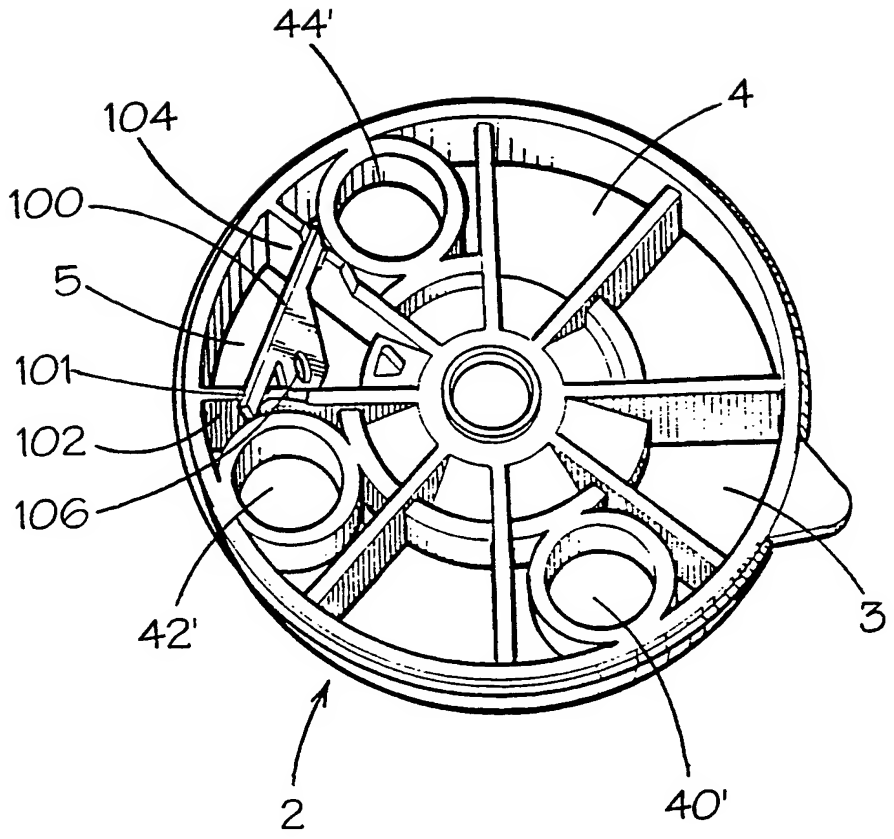

FIG. 3.

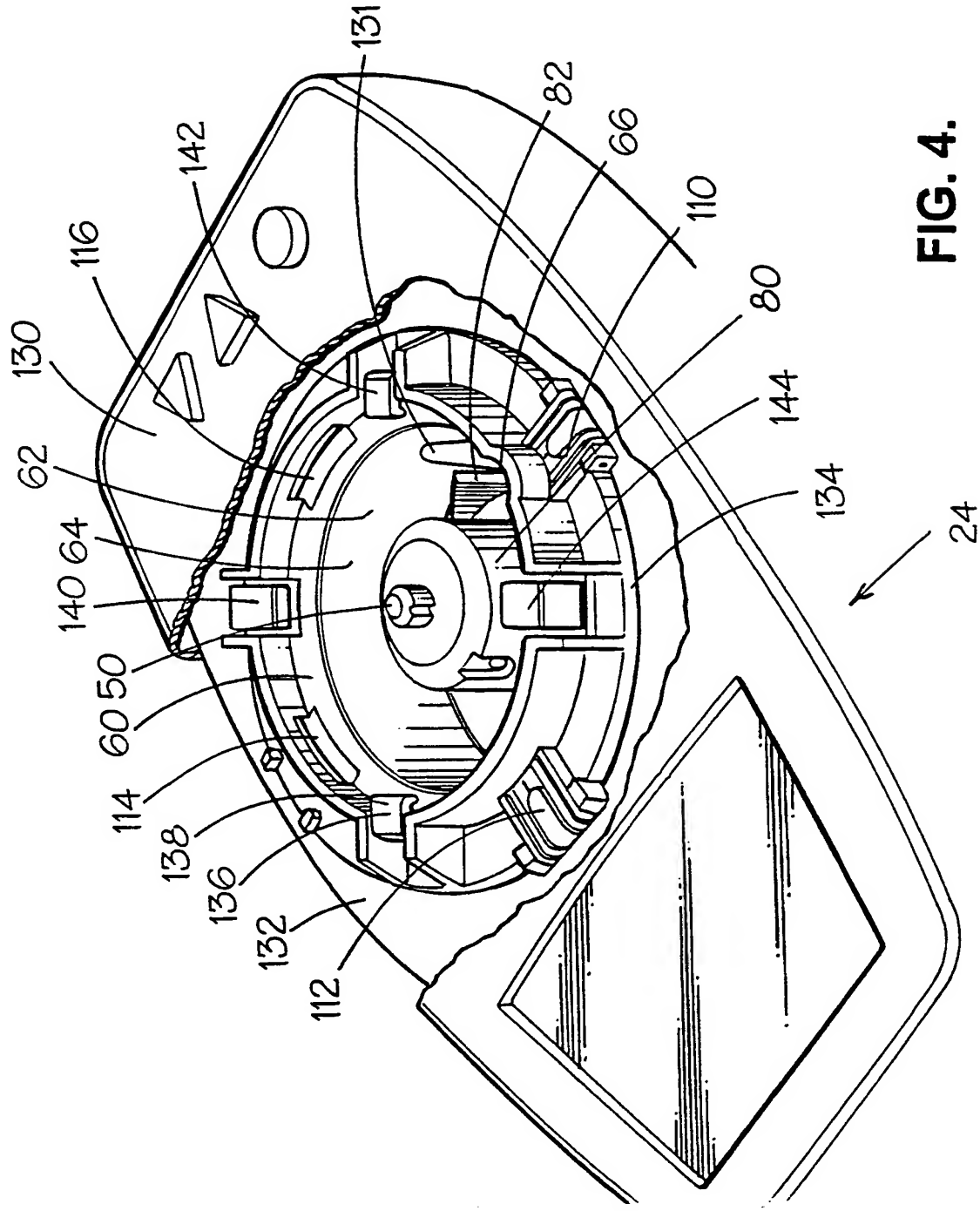
131
82
66
142
110
116
80
130
144
62
134
64
24
140
50
60
114
138
136
132
112

FIG. 4.

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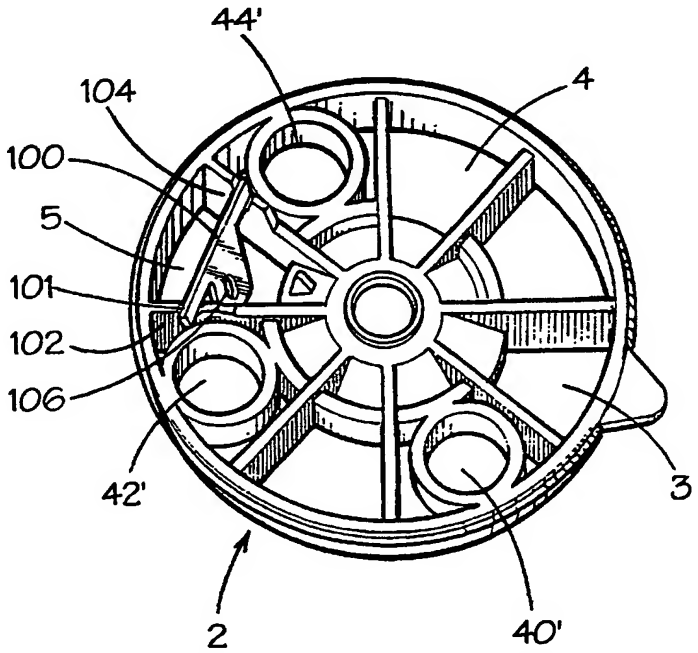
[Continued on next page]

(54) Title: MIXING APPARATUS AND METHOD OF MIXING DURING CONDUCTING AN ASSAY



(57) Abstract: Apparatus, instrument, device and a method of mixing for conducting an assay. Apparatus (31) comprising a first and second inlet and an inlet port accommodating a filter and/or binder retaining means, the inlet port moveable relative to first and second inlets such that the port (9) can be brought into liquid communication with each inlet, and a sample chamber (3, 5) comprising a paddle (100) wich undergeos a reciprocating motion.

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 283 141 A (STOCKDALE TREVOR J ET AL) 11 August 1981 (1981-08-11) the whole document ---	1-4,6-9, 12,15, 19,22,35
A	US 5 272 092 A (HAMASAKI FUMITOSHI ET AL) 21 December 1993 (1993-12-21) the whole document ---	1,2,4,6, 9,12, 15-17, 19,20, 22,35
A	US 3 356 346 A (K. LANDSBERGER) 5 December 1967 (1967-12-05) the whole document --- -/--	1,2,6, 10,12, 16,19, 20,22

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	US 4 612 291 A (DAWES DENNIS K) 16 September 1986 (1986-09-16) the whole document	1,2,6, 10-12, 19-21
A,P	WO 99 28038 A (ATTRIDGE JOHN WORTHINGTON ;CORTECS DIAGNOSTICS LIMITED (GB); STEVE) 10 June 1999 (1999-06-10) cited in the application the whole document	1-22,35
P,X	page 22, paragraph IX page 27, line 2 - line 4	30
P,A	page 25, line 8 - line 10; figures 5-9	23
A	EP 0 339 277 A (MILES INC) 2 November 1989 (1989-11-02) column 26, line 12 - line 19; figures	23
X	US 4 947 695 A (LOHR WILLY) 14 August 1990 (1990-08-14)	23-25,28
Y	column 4, line 39 - line 63; figures	26,27
Y	US 4 533 641 A (HOLT JOHN K) 6 August 1985 (1985-08-06) column 4, line 36 -column 5, line 9	26,27
A	US 3 853 010 A (CHRISTEN U ET AL) 10 December 1974 (1974-12-10) column 6, line 35 -column 7, line 55; figures	26,27
A	US 4 541 291 A (CHURCHILL JOHN E ET AL) 17 September 1985 (1985-09-17) column 7, line 7 - line 65; figure 1	26,27
X	EP 0 033 543 A (HOFFMANN LA ROCHE) 12 August 1981 (1981-08-12) page 5, line 14 - line 19	30
X	page 4, line 6 - line 8	31
X	US 4 407 961 A (SANDERS JAMES L) 4 October 1983 (1983-10-04) column 4, line 45 -column 5, line 24	30
A	US 5 597 532 A (CONNOLLY JAMES) 28 January 1997 (1997-01-28) column 6, line 10 - line 11 column 12, line 29 - line 38	31

-/--

INTERNATIONAL SEARCH REPORT

In. ational Application No
PCT/GB 00/02259

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 914 023 A (PHILO ROGER) 3 April 1990 (1990-04-03) column 2, line 34 - line 51; claim 1	31
X	WO 98 43739 A (BIOSITE DIAGNOSTICS INC) 8 October 1998 (1998-10-08) page 15, line 9 - line 10 page 17, line 3 - line 29; figure 1A	32,33
X	US 4 254 083 A (COLUMBUS RICHARD L) 3 March 1981 (1981-03-03) column 1, line 35 -column 2, line 13 column 3, line 26 - line 47; claims 1,7	32,33

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/02259

Box I Obs rvations wh re certain claims wer found uns archabl (Continuation f item 1 f first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

R mark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-22,35

   Method of mixing a sample , paddle for mixing , sample container adapted to recieve the paddle , instrument adapted to recieve the sample container and device comprising the instrument for reading one or more samples

2. Claims: 23-29

   Device comprising an instrument for reading one or more samples with positioning of the one or more samples into a reading position

3. Claims: 30,31

   Method for determining the percentage glycation of blood

4. Claims: 32-34

   Apparatus incorporationg one or a plurality of means for breaking the surface tension of a drop leaving a first component part to enter a second component part of an apparatus

INTERNATIONAL SEARCH REPORT

Information on patent family members

In. ational Application No
PCT/GB 00/02259

Patent document cited in search r port	Publication date	Patent family member(s)	Publication dat
US 4283141 A	11-08-1981	GB 1595881 A	19-08-1981
		DE 2905234 A	06-09-1979
		FR 2416720 A	07-09-1979
		JP 54130081 A	09-10-1979
		SE 7901144 A	14-08-1979
US 5272092 A	21-12-1993	JP 1229974 A	13-09-1989
		JP 2585740 B	26-02-1997
		DE 3838361 A	24-05-1989
US 3356346 A	05-12-1967	NONE	
GB 2018147 A	17-10-1979	SU 797750 A	23-01-1981
		DE 2911115 A	11-10-1979
		FR 2421670 A	02-11-1979
		JP 1431559 C	24-03-1988
		JP 55003887 A	11-01-1980
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US 4612291 A	16-09-1986	NONE	
WO 9928038 A	10-06-1999	AU 1493899 A	16-06-1999
		EP 1034039 A	13-09-2000
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EP 0339277 A	02-11-1989	US 4990075 A	05-02-1991
		AU 3256489 A	12-10-1989
		CA 1330197 A	14-06-1994
		DE 68901632 D	02-07-1992
		JP 2022560 A	25-01-1990
		JP 2711354 B	10-02-1998
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US 4947695 A	14-08-1990	DE 8816086 U	09-02-1989
		AT 97742 T	15-12-1993
		DE 58906261 D	05-01-1994
		EP 0375879 A	04-07-1990
US 4533641 A	06-08-1985	US 4454095 A	12-06-1984
US 3853010 A	10-12-1974	GB 1469172 A	30-03-1977
US 4541291 A	17-09-1985	GB 2125962 A	14-03-1984
		AU 559592 B	12-03-1987
		AU 1806783 A	23-02-1984
		DE 3364379 D	07-08-1986
		EP 0103329 A	21-03-1984
		JP 1629371 C	20-12-1991
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EP 0033543 A	12-08-1981	CA 1146769 A	24-05-1983
		DE 3167992 D	14-02-1985
		JP 56122959 A	26-09-1981
US 4407961 A	04-10-1983	NONE	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 00/02259

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5597532 A	28-01-1997	DE 69511533 D	23-09-1999
		DE 69511533 T	27-04-2000
		EP 0750739 A	02-01-1997
		WO 9613707 A	09-05-1996
US 4914023 A	03-04-1990	AT 93321 T	15-09-1993
		AU 601434 B	13-09-1990
		AU 7405987 A	17-12-1987
		CA 1284104 A	14-05-1991
		DE 3787051 A	23-09-1993
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		ES 2046203 T	01-02-1994
		IL 82790 A	30-06-1991
		JP 1986583 C	08-11-1995
		JP 7018877 B	06-03-1995
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WO 9843739 A	08-10-1998	AU 6579098 A	22-10-1998
		EP 1019193 A	19-07-2000
US 4254083 A	03-03-1981	AT 1366 T	15-08-1982
		CA 1129498 A	10-08-1982
		DE 2963436 D	16-09-1982
		EP 0010456 A	30-04-1980

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REC'D 20 SEP 2001

WIPO

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P400546WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02259	09/06/2000	10/06/1999
International Patent Classification (IPC) or national classification and IPC B01F13/08		
Applicant PROVALIS DIAGNOSTICS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/01/2001	18.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Degen, M Telephone No. +49 89 2399 8612

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02259

I. Basis of the r p rt

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-18 as originally filed

Claims, No.:

1-35 as originally filed

Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:
   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-5, 10, 11, 14, 16-22, 26-29, 34, 35
	No:	Claims	1, 6-9, 12, 13, 15, 23-25, 30-33
Inventive step (IS)	Yes:	Claims	34
	No:	Claims	1-33, 35

Industrial applicability (IA)	Yes:	Claims	1-35
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1: US-A-4 283 141 (STOCKDALE TREVOR J ET AL) 11 August 1981 (1981-08-11)

D2: WO 99 28038 A (ATTRIDGE JOHN WORTHINGTON ;CORTECS DIAGNOSTICS LIMITED (GB); STEVE) 10 June 1999 (1999-06-10) cited in the application

D3: US-A-4 947 695 (LOHR WILLY) 14 August 1990 (1990-08-14)

D4: US-A-4 533 641 (HOLT JOHN K) 6 August 1985 (1985-08-06)

D5: US-A-4 407 961 (SANDERS JAMES L) 4 October 1983 (1983-10-04)

D6: WO 98 43739 A (BIOSITE DIAGNOSTICS INC) 8 October 1998 (1998-10-08)

Re Item IV

Lack of unity of invention

1. This International Preliminary Examination Authority found multiple (groups of) inventions in this international application as follows:

A Claims 1-22

The subject matter of independent claims 1, 6, 12, 22 and respective dependent claims is concentrated on a mixing method/apparatus with the provision of a paddle which undergoes into a reciprocating motion.

B Claims 23-29

The subject matter of independent claim 23 and respective dependent claims is concentrated on a device allowing the reading of samples after determining the position of the samples using a "two-phased" recognition.

C Claims 30, 31

The subject matter of independent claim 30 and respective dependent claim 31 is concentrated on method for determining the percentage glycation of blood by spectrophotometry within a specific wave length.

D Claims 32-34

The subject matter of independent claim 32 and respective dependent claims 33, 34 is concentrated on "plurality of means for breaking the surface tension

of a drop" in order that the drop can leave a compartment of an apparatus to enter a second adjacent compartment of said apparatus.

E Claim 35

The subject matter of independent claim 35 is concentrated on the way of holding firmly an apparatus on an instrument using "spring clips".

2. The present application à priori does not fulfil the requirements of Rule 13.1 PCT, since neither the combination of essential features nor the inherent problems to be solved (and consequently also the corresponding solutions thereof) of the group of inventions are so linked as to form a single general inventive concept. Furthermore there is no technical connection within the solutions of the different inventions which gives expression to common inventive features.

Re Item V and VIII

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statem nt. Certain observations on the international application.

I. Invention A (Claims 1-22)

I.1 Clarity (Article 6 PCT)

The subject-matter for which protection is sought is not clearly defined in **claim 6**: it is not clear if the paddle, means for supporting the paddle, the chamber or a combination thereof are meant. Apparently, this claim should better be read as "a chamber comprising a paddle and means for supporting the paddle...".

In view of the above interpretation, and as a matter of conciseness, it would appear appropriate to recast independent **claim 12** as a dependent claim: "A sample container comprising a chamber according to claim 6".

As a matter of conciseness, unnecessary repetition of already claimed features should be replaced by the claim number referring to these features.

Reference signs placed in parentheses (Rule 6.2(b) PCT) are missing. The claims are therefore not clear.

I.2 Novelty (Article 33(2) PCT)

Document **D1** (Fig.1, claim 1) shows a *sample container comprising a chamber adapted to receive a paddle* which undergoes reciprocating motion and a *method of mixing a sample in a chamber comprising positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.*

The subject-matter of **claims 1, 6-9 and 12, 13, 15** is therefore not novel.

I.3 Inventive Step (Article 33(3) PCT)

The same document **D1** shows that the apparatus comprises an instrument capable of detecting an analyte in a sample in said sample container. However, the reciprocating motion of the stirrer is not initiated by said instrument. To add this feature to the apparatus of **D1** would be a normal practice for the skilled man who wants to automatize the complete analysis sequence. The subject-matter of **claim 22** is therefore not inventive.

Dependent **claims 2-5, 10, 11, 14 and 16-21**, do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

II. Invention B (Claims 23-29)

II.1 Clarity (Article 6 PCT)

The subject-matter for which protection is sought is not clearly defined in **claim 23**: it is not clear if *a device* contains *the instrument and an apparatus for presenting one or more samples,* if the device contains only the reading instrument being the apparatus independent from the device, or if the device corresponds to the instrument and includes the apparatus.

Following considerations are based on the latter interpretation.

II.2 Novelty (Article 33(2) PCT)

Document **D3** (Fig. 1-3; col. 4, lines 18-68) shows *a device* (Fig.1), *comprising an instrument for reading one or more samples*, including *an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.* The subject-matter of **claims 23-25** is therefore not novel.

II.3 Inventive Step (Article 33(3) PCT)

Dependent **claims 26-29** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step being merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the specific technical problem posed. In this respect document **D4** (Fig.1, 2; col.4, line 56 - col.5, line 9) shows an instrument including an apparatus for presenting one or more samples where the exact position of the sample is achieved by using two (mechanical) limit switches (54, 56).

III. Invention C (Claims 30-31)

The subject-matter of **claims 30-31** is not novel as a method for determining the percentage of glycation of blood is already known from document **D5** (column 1, lines 8-10; column 4, lines 48-53).

IV. Invention D (Claims 32-34)

IV.1 Clarity (Article 6 PCT)

Reference signs placed in parentheses (Rule 6.2(b) PCT) are missing. The claims are therefore not clear.

IV.2 Novelty (Article 33(2) PCT)

Document **D6** (page 7, line 26 - page 8, line 5; fig. 1A; page 17, lines 21-24; fig. 14) shows *an apparatus incorporating one or a plurality of means* (grooves, web) *for breaking the surface tension of a drop to ensure it leaves a first component part* (fig. 1A(2)) *and enters a second component part* (fig.1A(4)) *of an apparatus*. The subject-matter of **claims 32 and 33** is therefore not novel.

IV.3 Inventive Step (Article 33(3) PCT)

An apparatus comprising an inlet port being *a funnel and accommodating a filter means or binder retaining means*, as claimed in **claim 34** solves the problem to provide an easy to use and compact device which allows rapid and easy sample treatment. The solution to this problem as proposed in **claim 34** is neither known

from, nor suggested by available prior art and is therefore considered as involving an inventive step.

V. Invention E (Claim 35)

The subject-matter of **claim 35** is not considered to involve any inventive step (Article 33(3) PCT) as it would be obvious for the skilled man to provide a fixing means to hold a sample container firmly to a reading instrument in order to avoid false readings. An example of sample fixing is already shown in document **D3** (fig. 1).

ENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/02259	09/06/2000	10/06/1999
Applicant		
PROVALS DIAGNOSTICS LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

MIXING APPARATUS AND METHOD OF MIXING DURING CONDUCTING AN ASSAY

5. With regard to the **abstract,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 3

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[X] because this figure better characterizes the invention.

[ ] None of the figures.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

It is to be added references in parentheses as follows:
- line 3: Apparatus (31) comprising...
- line 5: ... that the port (9)...
- line 6: ... a sample chamber (3, 5)...
- line 7: a paddle (100)...

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/02259

Box I Observations where certain claims were found unsearchabl (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

R mark n Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied th payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-22,35

   Method of mixing a sample , paddle for mixing , sample container adapted to recieve the paddle , instrument adapted to recieve the sample container and device comprising the instrument for reading one or more samples

2. Claims: 23-29

   Device comprising an instrument for reading one or more samples with positioning of the one or more samples into a reading position

3. Claims: 30,31

   Method for determining the percentage glycation of blood

4. Claims: 32-34

   Apparatus incorporationg one or a plurality of means for breaking the surface tension of a drop leaving a first component part to enter a second component part of an apparatus

INTERNATIONAL SEARCH REPORT

International Application No
GB 00/02259

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01F13/08 B01F13/00 G01N1/38 G01N33/72

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01F G01N B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 283 141 A (STOCKDALE TREVOR J ET AL) 11 August 1981 (1981-08-11) the whole document ---	1-4,6-9, 12,15, 19,22,35
A	US 5 272 092 A (HAMASAKI FUMITOSHI ET AL) 21 December 1993 (1993-12-21) the whole document ---	1,2,4,6, 9,12, 15-17, 19,20, 22,35
A	US 3 356 346 A (K. LANDSBERGER) 5 December 1967 (1967-12-05) the whole document ---	1,2,6, 10,12, 16,19, 20,22

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 November 2000	04.01.2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hocquet, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]GB 00/02259

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 018 147 A (G SOJUZ Z MEK I KHIM OCHISTKE) 17 October 1979 (1979-10-17) the whole document	1-3,6,7, 10,12-14
A	US 4 612 291 A (DAWES DENNIS K) 16 September 1986 (1986-09-16) the whole document	1,2,6, 10-12, 19-21
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2

INTERNATIONAL SEARCH REPORT

International Application No
GB 00/02259

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

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International Application No
GB 00/02259

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P400546WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02259	09/06/2000	10/06/1999
International Patent Classification (IPC) or national classification and IPC B01F13/08		
Applicant PROVALIS DIAGNOSTICS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/01/2001	18.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Degen, M Telephone No. +49 89 2399 8612

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02259

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-18 as originally filed

Claims, No.:

1-35 as originally filed

Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:
see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 2-5, 10, 11, 14, 16-22, 26-29, 34, 35
	No:	Claims 1, 6-9, 12, 13, 15, 23-25, 30-33
Inventive step (IS)	Yes:	Claims 34
	No:	Claims 1-33, 35

Industrial applicability (IA) Yes: Claims 1-35
No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1: US-A-4 283 141 (STOCKDALE TREVOR J ET AL) 11 August 1981 (1981-08-11)

D2: WO 99 28038 A (ATTRIDGE JOHN WORTHINGTON ;CORTECS DIAGNOSTICS LIMITED (GB); STEVE) 10 June 1999 (1999-06-10) cited in the application

D3: US-A-4 947 695 (LOHR WILLY) 14 August 1990 (1990-08-14)

D4: US-A-4 533 641 (HOLT JOHN K) 6 August 1985 (1985-08-06)

D5: US-A-4 407 961 (SANDERS JAMES L) 4 October 1983 (1983-10-04)

D6: WO 98 43739 A (BIOSITE DIAGNOSTICS INC) 8 October 1998 (1998-10-08)

Re Item IV

Lack of unity of invention

1. This International Preliminary Examination Authority found multiple (groups of) inventions in this international application as follows:

A Claims 1-22

The subject matter of independent claims 1, 6, 12, 22 and respective dependent claims is concentrated on a mixing method/apparatus with the provision of a paddle which undergoes into a reciprocating motion.

B Claims 23-29

The subject matter of independent claim 23 and respective dependent claims is concentrated on a device allowing the reading of samples after determining the position of the samples using a "two-phased" recognition.

C Claims 30, 31

The subject matter of independent claim 30 and respective dependent claim 31 is concentrated on method for determining the percentage glycation of blood by spectrophotometry within a specific wave length.

D Claims 32-34

The subject matter of independent claim 32 and respective dependent claims 33, 34 is concentrated on "plurality of means for breaking the surface tension

of a drop" in order that the drop can leave a compartment of an apparatus to enter a second adjacent compartment of said apparatus.

E **Claim 35**
The subject matter of independent claim 35 is concentrated on the way of holding firmly an apparatus on an instrument using "spring clips".

2. The present application à priori does not fulfil the requirements of Rule 13.1 PCT, since neither the combination of essential features nor the inherent problems to be solved (and consequently also the corresponding solutions thereof) of the group of inventions are so linked as to form a single general inventive concept. Furthermore there is no technical connection within the solutions of the different inventions which gives expression to common inventive features.

Re Item V and VIII
Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statem nt. Certain observations on the international application.

I. **Invention A (Claims 1-22)**

I.1 Clarity (Article 6 PCT)
The subject-matter for which protection is sought is not clearly defined in **claim 6**: it is not clear if the paddle, means for supporting the paddle, the chamber or a combination thereof are meant. Apparently, this claim should better be read as "a chamber comprising a paddle and means for supporting the paddle...".

In view of the above interpretation, and as a matter of conciseness, it would appear appropriate to recast independent **claim 12** as a dependent claim: "A sample container comprising a chamber according to claim 6".
As a matter of conciseness, unnecessary repetition of already claimed features should be replaced by the claim number referring to these features.

Reference signs placed in parentheses (Rule 6.2(b) PCT) are missing. The claims are therefore not clear.

I.2 Novelty (Article 33(2) PCT)

Document **D1** (Fig.1, claim 1) shows a *sample container comprising a chamber adapted to receive a paddle* which undergoes reciprocating motion and a *method of mixing a sample in a chamber comprising positioning a paddle in the sample and causing said paddle to undergo a reciprocating motion.*
The subject-matter of **claims 1, 6-9 and 12, 13, 15** is therefore not novel.

I.3 Inventive Step (Article 33(3) PCT)

The same document **D1** shows that the apparatus comprises an instrument capable of detecting an analyte in a sample in said sample container. However, the reciprocating motion of the stirrer is not initiated by said instrument. To add this feature to the apparatus of **D1** would be a normal practice for the skilled man who wants to automatize the complete analysis sequence. The subject-matter of **claim 22** is therefore not inventive.

Dependent **claims 2-5, 10, 11, 14 and 16-21**, do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

II. Invention B (Claims 23-29)

II.1 Clarity (Article 6 PCT)

The subject-matter for which protection is sought is not clearly defined in **claim 23**: it is not clear if *a device* contains *the instrument and an apparatus for presenting one or more samples,* if the device contains only the reading instrument being the apparatus independent from the device, or if the device corresponds to the instrument and includes the apparatus.
Following considerations are based on the latter interpretation.

II.2 Novelty (Article 33(2) PCT)

Document **D3** (Fig. 1-3; col. 4, lines 18-68) shows *a device* (Fig.1), *comprising an instrument for reading one or more samples,* including *an apparatus for presenting the one or more samples to the instrument, wherein the positioning of the one or more samples into a reading position is achieved using two phased recognition.* The subject-matter of **claims 23-25** is therefore not novel.

II.3 Inventive Step (Article 33(3) PCT)

Dependent **claims 26-29** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step being merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the specific technical problem posed. In this respect document **D4** (Fig.1, 2; col.4, line 56 - col.5, line 9) shows an instrument including an apparatus for presenting one or more samples where the exact position of the sample is achieved by using two (mechanical) limit switches (54, 56).

III. Invention C (Claims 30-31)

The subject-matter of **claims 30-31** is not novel as a method for determining the percentage of glycation of blood is already known from document **D5** (column 1, lines 8-10; column 4, lines 48-53).

IV. Invention D (Claims 32-34)

IV.1 Clarity (Article 6 PCT)

Reference signs placed in parentheses (Rule 6.2(b) PCT) are missing. The claims are therefore not clear.

IV.2 Novelty (Article 33(2) PCT)

Document **D6** (page 7, line 26 - page 8, line 5; fig. 1A; page 17, lines 21-24; fig. 14) shows *an apparatus incorporating one or a plurality of means* (grooves, web) *for breaking the surface tension of a drop to ensure it leaves a first component part* (fig. 1A(2)) *and enters a second component part* (fig.1A(4)) *of an apparatus*. The subject-matter of **claims 32 and 33** is therefore not novel.

IV.3 Inventive Step (Article 33(3) PCT)

An apparatus comprising an inlet port being *a funnel and accommodating a filter means or binder retaining means*, as claimed in **claim 34** solves the problem to provide an easy to use and compact device which allows rapid and easy sample treatment. The solution to this problem as proposed in **claim 34** is neither known

from, nor suggested by available prior art and is therefore considered as involving an inventive step.

V. Invention E (Claim 35)

The subject-matter of **claim 35** is not considered to involve any inventive step (Article 33(3) PCT) as it would be obvious for the skilled man to provide a fixing means to hold a sample container firmly to a reading instrument in order to avoid false readings. An example of sample fixing is already shown in document **D3** (fig. 1).